Pancreatic Cancer Incidence, Mortality, and Survival in the SEER 17 Southern and Total United States (2000-2008)

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Abstract

Background: There is a paucity of data comparing the rates and time trends of pancreatic cancer in the southern and the total United States (US), as the risk factors for this cancer are disproportionately distributed in these two regions. The aim of this study was to compare the burden of this fatal cancer in these large geographic regions.

Methods: Age-adjusted incidence and mortality rates for patients (≥ 40 years) diagnosed with pancreatic cancer between 2000 and 2008 were calculated using the SEER 17 (southern and total US) data. Joinpoint regression was utilized to test the relationships between time and pancreatic cancer estimates. Relative, cause-specific, and conditional survival rates were also calculated for those diagnosed between 2000 and 2007.

Results: For both the study regions, an increase in incidence and mortality rates was observed in the older age groups (≥ 60 years), males, and blacks. The overall mortality rate in the southern states was slightly higher (26%) compared to the total US states (25%), with similar incidence rates observed in the two regions (27%). The annual percent increase (APC) in incidence rates was significant for all races and females in the southern states, but for all races and both the sexes in the total US. White females and black males in the southern states had higher three and five-year relative survival rates compared to their counterparts in the total US states.

Conclusion: Region-specific similarities and differences in incidence, mortality, and survival for pancreatic cancer were observed in the two regions. Particularly for the southern states, white females were at a significantly higher risk for developing this aggressive cancer compared to their male counterparts, and the incidence rate dramatically decreased for Asian/Pacific Islanders compared to other race/ethnic groups. These findings could have implications regarding preventive care services and treatment options for particular subgroups in the south.

Keywords: Pancreatic cancer, incidence, trends, mortality, relative survival, SEER Cancer Registries

Introduction

Pancreatic cancer is the fourth leading cause of cancer-related deaths among both males and females in the western world [1]. The international incidence rates of pancreatic cancer vary from five to ten cases per 100,000 a year [2], and it is more common in the developed countries compared to the developing countries [3]. In the United States, pancreatic cancer is projected to surpass other leading cancers such as breast and prostate cancers to become the second leading cause of cancer by 2030 [4].

Pancreatic cancer has one of the lowest five-year relative survival rates (6%), where the majority of pancreatic cancer patients die within one year from diagnosis [1,4]. Some of the

reasons for this poor prognosis are (i) inadequate screening procedures [2,5], (ii) ineligibility of cancer patients for surgery [6], (iii) potential risk of other organ damage during surgery [2], (iv) limited treatment options for metastatic pancreatic cancer, and (v) the inability of prompt detection of cancer among early-stage patients [4,7].

The few well-known risk factors of pancreatic cancer are age, smoking, and chronic pancreatitis [2,8]. Some other factors associated with pancreatic cancers are excess alcohol consumption, coffee drinking, diabetes mellitus, peptic ulcer disease, obesity, *H. pylori*, gender, race/ethnicity, marital status, insurance status, and aspirin use [2,7,11-14].

It is important to look at region-specific estimates for pancreatic cancer as the southern US states have distinct gender, racial/ethnic, social, and environmental factors influencing disease outcomes compared to other regions in the US. For instance, some of the southern states (e.g., Louisiana, Mississippi) have the highest prevalence of obesity in the US, which could be the consequence of low socioeconomic status and unhealthy dietary patterns in these states [15-18], and black men living in the southern states are more likely to be obese compared to the other states [13]. Additionally, with the exception of Texas, numerous states in the south have some of the lowest median household incomes per year [19], a finding corroborated with 12 southern states (e.g., Louisiana, Georgia) having the highest rates of low income students in public school attendance [20].

Pancreatic cancer estimates on incidence, mortality, and relative survival in the general US population have been reported previously [15,21]. To our knowledge, no studies have been conducted to shed light on these risk estimates in the southern region of the US, and hence, comparisons could not be made using incidence and mortality to identify the high-risk population in the southern region. For both the regions, the aims of this study were to: (i) calculate the overall, gender, age, and race-specific incidence and mortality rates for 2000 to 2008; (ii) estimate race and gender-specific relative, cause-specific, and conditional survivals for the patients diagnosed with pancreatic cancer between 2000 and 2007; and (iii) explore the trends in the age-adjusted incidence and mortality rates for 2000 to 2008 using the population-based Surveillance, Epidemiology, and End Results (SEER) program registries.

Methods

Description of SEER Data/Study Population

This study utilized publicly available data from the Surveillance, Epidemiology, and End Results (SEER) program. The program is a population-based cancer registry that aims to cover approximately one quarter of the US population. The cancer cases are reported to the registry from different US regions, and is a source of the most comprehensive incidence and mortality data available to date for various types of cancers prevalent in the United States [22]. The analysis was restricted to the SEER 17 [23] cancer registry to restrict the analysis to the southern United States (Atlanta, Rural Georgia, Louisiana, and Kentucky) and the total US for patients that were diagnosed with pancreatic cancer between 2000 and 2008 that were ≥ 40 years.

Statistical Analysis

Race, age, and gender-specific age-adjusted incidence and mortality rates for patients diagnosed with pancreatic cancer between 2000 and 2008 were calculated using the SEER program [22]. Trend analyses were performed to calculate the Annual Percent Change (APC) in the incidence and mortality rates. The APC is a way to understand cancer rates over time, where the rates are assumed to increase at a constant rate from the past year. It is also a measure that is comparable across many

scales to compare rare and common types of cancers [24]. The incidence and mortality rates were age-standardized using the 2000 standard US population. Linear regression models were fit to test for linear relationships between time (in years) and pancreatic cancer estimates (incidence and mortality). Joinpoint regression model was utilized to test for non-linear relationship using the Joinpoint Regression Program [25].

For cases diagnosed between 2000 and 2007, the relative, cause-specific, and conditional survivals were calculated. These estimates were calculated for whites and blacks only as the life tables used to calculate the expected survival for other races such as Asians, Pacific Islanders, and Native Americans are not accurate [26]. The relative survival of pancreatic cancer was calculated as a ratio of the proportion of the observed survivors to the proportion of expected survivors. It estimates the effect of a health outcome (e.g., pancreatic cancer) in the absence of competing risks or other causes of death [26]. Conditional survival is a measure of probability of a cohort surviving further than the year of interest, given that the person has survived up to the year of interest after the diagnosis of a disease. It provides valuable information regarding a patient's prognosis for long-term survival [27]. Cancer-specific or cause-specific survival is a net survival from a specific cause or disease (e.g., pancreatic cancer) in the absence of competing causes of death [26].

Results

Tables 1 and 2 demonstrate the age-adjusted incidence and mortality rates of pancreatic cancer in the SEER 17 southern states and total US, respectively. From 2000 to 2008, there were a total of 11, 273 incident cases and 10,727 deaths reported in the southern states, as compared to the 75, 685 incident cases and 285,696 deaths reported in the total US states. The incidence rates between these two regions did not differ, but the mortality rate in the southern states was slightly higher (25.5 per 100,000) than the total US (24.7 per 100,000). The incidence and mortality rates were higher among males, older age groups (≥ 60 years) and blacks compared to their counterparts in both of the regions.

The overall three-year survival rates between the two regions did not vary significantly from 2000 to 2007; however, the overall five-year survival rate for the southern states was slightly higher compared to the total US states. Similar patterns in three- and five-year survivals were observed for both the genders and all races between the regions (Table 3). Even though the overall three-year cause-specific survival was higher for the US total states, a reversal in pattern was observed in the five-year cause-specific survival (Table 4). Total US black females had a notable increase in three-year cause-specific survival compared to the southern black females. On the contrary, southern white females had a higher five-year cause-specific survival compared to the total US white females (Table 4).

Temporal trends in age-standardized pancreatic cancer incidence and mortality rates for the SEER 17 southern states and total US are depicted by Figures 1 and 4. A significant increase in pancreatic incident rate was observed among all races and all females

Table 1. Age-adjusted incidence rates of malignant pancreatic cancer in the SEER 17 southern and total states (2000-2008).

Variable of Interest	Southern United States			Total	Total United States			Total
	Incident Cases	Incidence Rate*	95% CI		Incident Cases	Incidence Rate*	95% CI	
Overall	11,273	27.1	(26.6, 27.6)	44,709,963	75,685	27.1	26.8, 27.2	291,552,608
Age at Diagnosis								
40-49	695	4.3	(4.0, 4.6)	16,019,258	3,965	3.8	(3.6, 3.9)	103,900,678
50-59	1,881	14.6	(13.9, 15.3)	12,811,739	11,302	13.7	(13.5, 14.0)	81,684,618
60-69	2,788	36.3	(35.0, 37.7)	7,775,485	17,234	35.5	(35.0, 36.1)	49,302,933
70-79	3,311	65.0	(62.7, 67.2)	5,105,235	22,691	65.7	(64.8, 66.5)	34,514,796
80+	2,598	86.7	(83.4, 90.1)	2,998,246	20,403	92.3	(91.0, 93.5)	22,119,583
Gender								
Male	5,544	30.9	(30.1, 31.8)	20,807,228	37,180	30.7	(30.4, 31.0)	137,555,475
Female	5,729	23.9	(23.3, 24.5)	23,902,735	38,505	24.1	(23.8, 24.3)	153,967,133
Race†								
White	8,654	25.6	(25.1, 26.2)	34,550,626	62,149	26.7	(26.5, 26.9)	234,835,438
Black	2,513	34.8	(33.4, 36.2)	9,177,685	8,106	35.8	(35.0, 36.6)	27,639,558
American Indians/ Alaskan Natives	11	8.9	(4.3, 16.4)	166,443	406	17.6	(15.9, 19.5)	3,088,119
Asian Americans/ Pacific Islanders	90	18.7	(14.5, 23.5)	815,210	4,803	21.5	(20.9, 22.1)	25,959,494

*Incidence rates are per 100,000 and age-adjusted to 2000 US standard population; rates calculated for persons 40 years and older.

Table 2. Age-adjusted mortality rates of pancreatic cancer in the SEER 17 southern and total states (2000-2008).

Variable of Interest	Southern United States			Total	Total United States			Total
	Number of Deaths	Mortality Rate*	95%CI (Upper CI, Lower CI)		Number of Deaths	Mortality Rate*	95%CI (Upper CI, Lower CI)	
Overall	10,727	25.5	25.0, 25.9	45,635,577	285,696	24.7	24.6, 24.8	1,164,952,027
Age at death								
40-49	552	3.3	(3.1, 3.6)	16,331,784	11,930	2.9	(2.9, 3.0)	398,991,966
50-59	1,554	11.8	(11.2, 12.4)	13,080,181	37,812	11.6	(11.5, 11.7)	323,246,269
60-69	2,514	32.2	(30.9, 33.5)	7,941,016	62,739	30.9	(30.7, 31.2)	204,842,095
70-79	3,259	62.6	(60.5, 64.8)	5,217,377	87,502	60.1	(59.7, 60.5)	145,397,271
80+	2,848	93.0	(89.6, 96.5)	3,065,219	85,713	92.7	(92.1, 93.3)	92,474,426
Gender								
Male	5,273	29.5	(28.7, 30.4)	21,236,132	140,680	28.5	(28.3, 28.7)	46,801,936
Female	5,454	22.2	(21.6, 22.8)	24,399,445	145,016	21.6	(21.5, 21.7)	618,150,091
Race								
White	8,246	24.1	(23.6, 24.6)	35,214,875	245,327	24.3	(24.2, 24.4)	984,932,912
Black	2,394	32.9	(31.6, 34.3)	9,422,465	33,109	32.0	(31.6, 32.3)	124,308,537
American Indians/ Alaskan Natives	17	14.3	(8.0, 23.4)	171,821	1,064	15.2	(14.2, 16.2)	9,509,224
Asian Americans/ Pacific Islanders	70	15.6	(11.7, 20.2)	826,416	6,196	17.3	(16.8, 17.7)	46,201,354

*Mortality rates are per 100,000 and age-adjusted to 2000 US standard population; rates calculated for persons 40 years and older.

in the southern states, but an increase in incidence rate was seen for all races, both genders in the total US (**Figures 1 and 4**). Also, a noteworthy increase in mortality rate was observed in the total US for all races and both the genders, but not in the southern states (**Figures 1 and 4**).

When the incident rates were compared among the different racial/ethnic groups between the two regions, white females had a significant increase in the incidence rate in the southern states (**Figure 2**), and such increase was noted for both white males and females in the total US (**Figure 5**). There was a dramatic

Table 3. Three and five-year relative survival rates (%) and confidence intervals for cases ≥40 years that were diagnosed between 2000 and 2007 (SEER 17 southern and total states).

	SEER 17 Southern States			SEER 17 Total States		
	N	3-year survival (CI)	5-year survival (CI)	N	3-year survival (CI)	5-year survival (CI)
Overall	8,021	7.1 (6.5, 7.7)	5.3 (4.8, 6.0)	51,774	7.2 (6.9, 7.4)	4.8 (4.5, 5.0)
Total Males	3,882	7.0 (6.1, 7.9)	5.2 (4.4, 6.1)	25,185	7.2 (6.8, 7.6)	4.7 (4.3, 5.0)
Total Females	4,139	7.2 (6.4, 8.1)	5.4 (4.6, 6.3)	26,589	7.1 (6.8, 7.5)	4.9 (4.5, 5.2)
Whites	6,098	7.4 (6.7, 8.1)	5.4 (4.8, 6.2)	42,367	7.2 (7.0, 7.5)	4.9 (4.6, 5.1)
Male	3,011	7.2 (6.2, 8.2)	5.2 (4.3, 6.2)	20,836	7.3 (6.9, 7.7)	4.8 (4.4, 5.2)
Female	3,087	7.6 (6.6, 8.7)	5.7 (4.7, 6.7)	21,531	7.2 (6.8, 7.6)	4.9 (4.5, 5.3)
Black	1,845	6.1 (5.0, 7.4)	5.0 (3.9, 6.3)	5,670	6.2 (5.5, 6.9)	4.0 (3.4, 4.7)
Male	829	6.1 (4.5, 8.0)	5.5 (3.9, 7.4)	2,521	5.6 (4.7, 6.7)	3.4 (2.6, 4.5)
Female	1,016	6.2 (4.7, 8.0)	4.7 (3.3, 6.4)	3,149	6.7 (5.7, 7.7)	4.5 (3.6, 5.4)

Table 4. Three and five-year cause-specific survival rates (%) and confidence intervals for cases ≥40 years that were diagnosed between 2000 and 2007 (SEER 17 southern and total states).

	SEER 17 Southern States			SEER 17 Total States		
	N	3-year survival (CI)	5-year survival (CI)	N	3-year survival (CI)	5-year survival (CI)
Overall	7,965	7.3 (6.7, 8.0)	5.7 (5.2, 6.4)	52,312	7.7 (7.5, 8.0)	5.3 (5.1, 5.5)
Total Males	3,855	7.3 (6.4, 8.2)	5.6 (4.8, 6.5)	25,540	7.8 (7.4, 8.1)	5.1 (4.8, 5.5)
Total Females	4,110	7.4 (6.5, 8.3)	5.9 (5.1, 6.7)	26,772	7.7 (7.3, 8.0)	5.5 (5.2, 5.8)
Whites	6,063	7.6 (6.9, 8.3)	5.9 (5.2, 6.6)	42,815	7.7 (7.4, 8.0)	5.3 (5.0, 5.5)
Male	2,995	7.4 (6.4, 8.5)	5.6 (4.7, 6.6)	21,138	7.8 (7.4, 8.2)	5.2 (4.8, 5.5)
Female	3,068	7.7 (6.7, 8.8)	6.1 (5.2, 7.2)	21,677	7.6 (7.2, 8.0)	5.4 (5.0, 5.7)
Black	1,826	6.5 (5.3, 7.8)	5.3 (4.2, 6.6)	5,755	7.1 (6.4, 7.9)	5.0 (4.3, 5.8)
Male	819	6.5 (4.9, 8.6)	5.5 (3.9, 7.5)	2,567	6.6 (5.5, 7.7)	4.1 (3.2, 5.2)
Female	1,007	6.5 (4.9, 8.3)	5.2 (3.7, 6.9)	3,188	7.6 (6.6, 8.6)	5.7 (4.8, 6.8)

decline in the incidence rate among Asian/Pacific Islander males in the southern states, but not in the total US (Figures 2 and 5). Regarding the mortality trends, no significant changes were observed in the rates for different racial/ethnic groups in the southern states (Figure 3); however, significant changes in mortality rates were observed for the whites (overall), and white males and females in the total US (Figure 6).

Discussion

This study documents the incidence and mortality rates of pancreatic cancer for the southern and the total US among adults 40 years and older. For the same population, temporal trends, and relative, conditional, cause-specific survivals were calculated to explore the underlying factors influencing morbidity and mortality outcomes in various subgroups.

The significant APC change in incidence in the southern states, particularly among whites, could be explained by two major factors. A large health disparity exists in the south; nearly one in five non-elderly southerners do not have health insurance where the largest uninsured group are whites (42%) compared to the other racial/ethnic groups [28]. Moreover, some southern

states have the highest poverty rates in the nation [19,20,28] contributing to some of the worse health outcomes and chronic illnesses compared to the rest of the nation [29].

Women are more likely to get their insurance as dependents compared to men, and their risk of losing health benefits increases if they become widowed, divorced, or if their spouses lose jobs through which insurance is provided [30]. This could be one of the key factors why women that are under 65 years are less likely to have health insurance coverage as compared to their counterparts [31]. Nonetheless, why the increase in APC is much higher in southern women compared to the overall women in the US, and especially among white women, needs to be further elucidated. Previous studies have informed that women generally survive longer in industrialized countries and utilize more health care services compared to their male counterparts [32-34]. Even though women in the south have one of the nation's lowest life-expectancies [35], the aforementioned factors could have impacted the increase in incidence rates of pancreatic cancer among females.

Another notable finding was the significant decrease in APC in incidence among male Asians/Pacific Islanders in the south;

^The Annual Percent Change (APC) is significantly different from zero at alpha = 0.05

Figure 1. Temporal trends in age-standardized pancreatic cancer incidence and mortality rates for the SEER 17 southern states, 2000 to 2008 (ages ≥ 40). Morality for Asians/Pacific Islanders and American Indians/Alaskan Natives are not shown due to low numbers. Rates are calculated per 100,000 and adjusted to the 2000 US standard population.

no such pattern was observed for the same ethnic group in the total US. Although the trends in incidence rates for black males in the south and the total US were inconsistent, the incidence rates for black females appeared to be rising (although not significantly) for the two regions, a finding consistent with what was seen for white females. This could indicate that females in the south, more than males as observed nationally, could be at risk for pancreatic cancer.

Consistent with the total US estimates, males and blacks in the southern states had higher incidence and mortality rates from 2000 to 2008 of pancreatic cancer compared to the females and other races respectively. This is also consistent with the presumed risk factors (e.g., pancreatitis, Vitamin D deficiency) that seem to be contributing to the incidence of pancreatic cancer [36,37]. The increase in incidence rates of pancreatic cancer observed among whites and blacks could be directly associated with their smoking and drinking behaviors [38]. However, the same association between smoking and pancreatic cancer was not observed among American Indians and Alaskan Natives.

This study should be interpreted in the context of some important limitations. Information on other covariates linked with pancreatic cancer such as smoking and excess alcohol consumption were not considered due to the nature of registry, and only age-adjusted estimates were reported. Additionally, there were a limited number of states that reported to SEER registries for the study period, which could compromise the generalizability of our findings as some of these SEER areas may not be representative of the total US population [39]. However, the SEER database provides an accurate representation of the US cancer population due to its large sample size and long follow-up period. Additionally, for quality control, each SEER registry is routinely audited for data accuracy, and registrars are frequently trained for complete case ascertainment and timely reporting [1]. There is also a possibility of selection bias due to migration and treatment options [40], but due to the high fatality rate of pancreatic cancer and limited treatment options, these biases are less likely to impact the calculated estimates.

This study has two important advantages that make it unique.

*The Annual Percent Change (APC) is significantly different from zero at $\alpha = 0.05$

Figure 2. Temporal trends in age-standardized pancreatic cancer incidence among White, Black, and Asian/Pacific Islander in SEER 17 southern states, 2000 to 2008 (ages ≥ 40). Rates are calculated per 100,000 and adjusted to the 2000 US standard population. Incidence for American Indian/Alaskan Native is not shown due to low numbers.

^aThe Annual Percent Change (APC) is significantly different from zero at alpha = 0.05

Figure 3. Temporal trends in age-standardized pancreatic cancer mortality among whites and blacks in the SEER 17 southern states, 2000 to 2008 (ages ≥ 40). Mortality for Asian/Pacific Islander and American Indian/Alaskan Native are not shown due to low numbers. Rates are calculated per 100,000 and adjusted to the 2000 US standard population.

^aThe Annual Percent Change (APC) is significantly different from zero at alpha = 0.05

Figure 4. Temporal trends in age-standardized pancreatic cancer incidence and mortality rates for the SEER 17 total states, 2000 to 2008 (ages ≥ 40). Rates are calculated per 100,000 and adjusted to the 2000 US standard population.

To our knowledge, there is scarce data on gender and race-specific pancreatic cancer incidence, mortality, and survival estimates in the US southern region. The present study is the first to calculate race and gender specific estimates of pancreatic cancer in the southern US, which could not be teased out by looking at the overall US estimates. Second, a standardized protocol was utilized to collect data from the participants [40]. Therefore, the reported estimates are likely valid and reliable.

In essence, this study demonstrated that the pancreatic cancer burden is increasing in the southern US for persons ≥ 40 years. Females and whites in the south seem to have higher risks of

developing this aggressive cancer annually compared to males and other racial groups nationally. These findings could have implications regarding preventive care services and treatment options for particular subgroups in the south. Therefore, clinicians and public health workers should combine their efforts to increase awareness about this cancer, especially among high risk individuals.

Competing interests

The author declares that she has no competing interests.

Authors' contributions

The listed author was solely responsible for the research

=^The Annual Percent Change (APC) is significantly different from zero at alpha = 0.05

Figure 6. Temporal trends in age-standardized pancreatic cancer mortality among Whites, Blacks, and Asian/Pacific Islanders in the SEER 17 total states, 2000 to 2008 (ages ≥ 40). Rates are calculated per 100,000 and adjusted to the 2000 US standard population.

design, analysis, and development of paper, and hence responsible for the final content of the manuscript.

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